Research In Cancer and Tumor 2026, 13(3): 35-38
DOI: 10.5923/j.rct.20261303.01

Benign and Malignant Mesenchymal Uterine Tumors: How Diagnostic Accuracy Varies Depending on the Type of Specimen Obtained

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Abstract **The aim** of the study was a comparative evaluation of the diagnostic efficiency of various methods for obtaining tissue samples from benign and malignant uterine tumors. In the current gynecologic oncology literature, the issue of preoperative morphological verification of uterine sarcomas remains one of the most challenging. The authors conducted comparative analysis of 137 patients aged 22 to 60 who were treated at the Department of Reproductive System Tumors of the Republican Specialized Scientific-Practical Medical Center of Oncology and Radiology for the period from 2015 to 2022 in terms of using different methods for obtaining tissue samples from benign and malignant uterine tumors. Some differences were observed in terms of morphological verification prior to treatment initiation, which was confirmed in 38.1% of patients with uterine sarcomas and in 17.0% of patients with leiomyoma (p=0.009). Based on the study, it can be concluded that a negative result of endometrial aspiration biopsy or SDC, in the presence of MRI/ultrasound findings suspicious for an intramural mass, should not serve as a basis for ruling out uterine sarcoma. On the contrary, this combination of results justifies the need for further comprehensive evaluation using imaging findings and, in carefully selected cases, obtaining tissue directly from the tumor.

Keywords Malignant mesenchymal uterine tumor, Uterine sarcoma, Leiomyoma

1. Introduction

Leiomyosarcoma, endometrial stromal sarcoma and other rare tumors differ in their origin and molecular basis; grouping them into a single morphological category may obscure important diagnostic distinctions, which can lead to diagnostic errors and subsequent consequences for treatment [1-2].

In the current gynecologic oncology literature, the issue of preoperative morphological verification of uterine sarcomas remains one of the most challenging. As sarcomas are often developed in the myometrium beneath an intact endometrium, traditional methods frequently yield false-negative results [3].

Leiomyomas are benign uterine smooth muscle tumors that are present in up to 8 out of 10 women by the age of 50. Many of these women experience symptoms such as heavy and irregular menstrual bleeding, early pregnancy loss, and infertility. Traditionally believed to be inert masses, fibroids are now known to influence endometrial function at the molecular level [4].

The main methods for obtaining material for histological and immunohistochemical examination are:

- Separate diagnostic curettage (SDC) of the uterine cavity and cervical canal, which involves instrumental curettage of the mucous membrane of the cervical canal and the uterine cavity;
- Endometrial aspiration biopsy (Pipelle biopsy): Collection of a sample from the surface layer of the endometrium using a flexible plastic tube (Pipelle) under negative pressure;
- Hysteroscopy with targeted biopsy: examination of the uterine cavity using an optical instrument (hysteroscope) with visual collection of samples of suspicious tissue;
- Tumor trephine biopsy (puncture biopsy) under ultrasound or CT guidance: percutaneous or transvaginal puncture of a large nodule or metastatic lesion using a thin or thick needle under visual guidance.

The aim of the study was a comparative evaluation of the diagnostic efficiency of various methods for obtaining tissue samples from benign and malignant uterine tumors.

2. Material and Methods

We conducted comparative analysis of 137 patients aged 22 to 60 who were treated at the Department of Reproductive System Tumors of the Republican Specialized Scientific-Practical Medical Center of Oncology and Radiology for the period from 2015 to 2022 from the point of view various

Received: Oct. 27; Accepted: Nov. 16, 2026; Published: Nov. 19, 2026
Published online at http://journal.sapub.org/rct

methods for obtaining tissue samples from benign and malignant uterine tumors. The patients were divided into two groups as follows:

The Main Group (n=84) with morphologically confirmed uterine sarcomas (UtS).

Control Group (n=53) with a histologically confirmed diagnosis of uterine leiomyoma (LM).

Inclusion criteria to the study were as follows:

- Female, age 18 and older;
- Examination and treatment at the institutions serving as clinical research sites during the period specified in the protocol;
- Presence of a morphologically confirmed primary uterine tumor: in the Main group—uterine sarcomas with an established histological subtype; in the Control group—benign uterine leiomyomas, including their morphological variants;
- Availability of medical records to identify key clinical and anamnestic characteristics, examination results, the nature of the procedure performed, and the final diagnosis;
- Availability of representative histological material from the primary tumor—including micro sections and/or paraffin blocks—for diagnostic review and morphological analysis;
- The availability and performance of immunohistochemical and molecular genetic stages of the study.

Exclusion criteria were as follows:

- Lack of morphological confirmation of the diagnosis/ inability to reliably distinguish between uterine sarcoma and benign leiomyoma;
- A smooth muscle tumor of uncertain malignant potential – STUMP;
- Other neoplasms not classified under the established diagnostic groups: carcinoma and carcinosarcoma of the uterus, metastatic lesions of the uterus, sarcoma of other primary sites, and other mesenchymal tumors;
- The absence/incomplete nature of medical documentation to confirm inclusion criteria and assessment of key study parameters;
- No material available to perform a reliable morphological verification;
- Conducting antitumor therapy prior to a reliable evaluation of the tumor's baseline morphological and biological characteristics.

Statistical processing of the clinical data was performed using the “EXCEL” and “STATGRAFICS” software packages (USA). The significance of the differences revealed in the analysis of quantitative traits was assessed using the Student-Fisher test. The methods of variation parametric and nonparametric statistics were used, including the calculation of the arithmetic mean (M) of the indicator under study, square mean deviation (σ), the standard error of the mean (m), and relative values (frequency, %). The statistical significance of the obtained measurements in comparing mean values was determined using the Student’s t-test, with the probability of error (p) calculated after testing for normality of distribution (using the kurtosis criterion) and equality of population variances (F-test). A significance level of $p < 0.05$ was used to determine statistically significant changes.

The “OpenEpi 2009, Version 2.3” software package was used as a computational tool for molecular genetic studies. Data analysis model: Case-control.

3. Results

From the perspective of pathological anatomy, preoperative verification should be further classified according to the method used to obtain the specimen: endometrial aspiration biopsy, separate diagnostic curettage, hysteroscopic biopsy, tumor trephine biopsy, or re-examination of previously prepared specimens. These methods provide varying degrees of diagnostic information, especially when the tumor is located intramurally (Table 1).

No significant differences were found in the structure of the methods used to obtain material prior to surgery between the UtS and LM groups ($p > 0.05$ for all methods), indicating that the groups were comparable in terms of the nature of the preoperative morphological examination.

Table 1. Methods of obtaining material for preoperative morphological examination

Method	UtS, (n=84), abs.	UtS %	LM, (n=53), abs.	LM, %	p*	UtS verification, n/N (%)
Endometrial aspiration biopsy	18	21.4	15	28.3	0.414	6/18 (33.3)
Separate diagnostic curettage (SDC)	24	28.6	17	32.1	0.704	10/24 (41.7)
Hysteroscopic biopsy	20	23.8	11	20.8	0.834	14/20 (70.0)
Tumor trephine biopsy	10	11.9	3	5.7	0.370	9/10 (90.0)
Re-examination of previously prepared specimens	12	14.3	7	13.2	1.000	10/12 (83.3)
Total	**84**	**100.0**	**53**	**100.0**	—	**49/84 (58.3)**

Note: * To compare the frequency of use of a specific method across groups—Fisher's exact test

Table 2. Diagnostic accuracy of various methods for obtaining tissue samples in uterine sarcomas

Method	Investigations, n	Informative material, n (%)	UtS verified, n (%)	Suspicion on malignant tumor, n (%)	Non-informative/false negative result, n (%)	Diagnostic sensitivity, %
Endometrial aspiration biopsy	18	11 (61.1)	6 (33.3)	5 (27.8)	7 (38.9)	33.3
SDC	24	17 (70.8)	10 (41.7)	7 (29.2)	7 (29.2)	41.7
Hysteroscopic biopsy	20	18 (90.0)	14 (70.0)	4 (20.0)	2 (10.0)	70.0
Tumor trephine biopsy	10	10 (100.0)	9 (90.0)	1 (10.0)	0	90.0
Re-examination of previously prepared specimens	12	12 (100.0)	10 (83.3)	2 (16.7)	0	83.3

Table 3. Diagnostic efficiency depending on tumor location

Method	Submucosal growth, verified (%)	Intramural growth, verified. (%)	Subserosal growth, verified. (%)	χ^2	P
Endometrial aspiration biopsy	6/8 (75.0)	1/8 (12.5)	0/2 (0)	8.01	0.018
SDC	8/10 (80.0)	2/10 (20.0)	0/4 (0)	10.83	0.004
Hysteroscopic biopsy	11/12 (91.7)	2/6 (33.3)	1/2 (50.0)	6.90	0.032
Tumor trephine biopsy	2/3 (66.7)	6/6 (100.0)	1/1 (100.0)	2.59	0.274

Table 4. What was the most informative aspect of each localization?

Tumor location	Preferred method	Calculated efficiency	Practical significance
Submucosal/intracavitary	Hysteroscopy + targeted biopsy	91.7%	The tumor is accessible for direct visualization and targeted biopsy
Intramural	Tumor trephine biopsy	100.0%	Endometrial biopsies often fail to reach the tumor tissue
Subserosal	Trephine biopsy with safe access and appropriate indications	-*	The endometrium is usually not involved
Tumor extending into the uterine cavity	Hysteroscopic biopsy	High	The procedure allows for the collection of tissue directly from the pathological area
Isolated intramural tumor	Aspirational biopsy/SDC are of little diagnostic value	12.5-20.0%	A negative result does not exclude the UtS

Note: * Due to the small sample size (n), it is not possible to calculate the true sensitivity of the method for the entire population

However, it should be noted that the efficiency of the methods varied significantly within the Main group. The lowest rate of direct morphological verification was observed during endometrial aspiration biopsy—33.3%, and it was slightly higher for SDC—41.7%. This is typical for mesenchymal tumors located within the myometrium: the endometrial tissue may not contain any tumor tissue at all. Hysteroscopic biopsy showed higher success rates—23.8% with UtS versus 20.8% with LM. For LM, SDC proved to be the most efficient—32.1%.

To evaluate the diagnostic efficiency of different methods for obtaining material at UtS, various methods allowing for "accurate verification" were studied. The results are presented in Table 2.

The data obtained show a marked correlation between diagnostic accuracy and the method used to collect the sample. Endometrial aspiration biopsy proved to be the least efficient - 33.3%, whereas the rate for SDC was 41.7%. The differences between these two methods are minor, suggesting that blind curettage offers no significant advantage over endometrial biopsy in the diagnosis of LMS.

In hysteroscopic targeted biopsy, the estimated diagnostic accuracy increased to 70.0%, while the proportion of non-informative or false-negative results decreased to 10.0%. Thus, if a tumor deforms the uterine cavity, has a submucosal component, or is visible during hysteroscopy, targeted sampling is preferable over blind SDC.

The highest success rate was achieved in trephine biopsy performed directly on the tumor mass—90.0%. However, based on this, we cannot recommend trephine biopsy for all patients, as the procedure requires appropriate indications, safe access to the tumor, and adherence to oncological principles.

The most important aspect of the study was the evaluation of how diagnostic accuracy varies depending on tumor location. The data obtained are presented in Table 3.

We evaluated the selection of the most informative method based on tumor location and examined their efficiency, the results of which are shown in Table 4.

The conducted analysis showed that the diagnostic

efficiency of endometrial methods depends on the anatomical location of the tumor. In cases of submucosal or intracavitary growth the efficiency of aspiration biopsy was 75.0% and that of SDC was 80.0%, while the highest rate was observed during hysteroscopic targeted biopsy—91.7%.

A completely different tendency was observed when the tumor was located intramurally: the efficiency of aspiration biopsy decreased to 12.5%, SDC - to 20.0%, hysteroscopic biopsy - to 33.3%. Conversely, obtaining material directly from the tumor mass provides a significantly higher probability of morphological verification. It is understandable from a pathophysiological perspective, as LMS is formed in the myometrium; therefore, a standard endometrial examination may not detect the tumor tissue.

In our study, the dependence of efficiency on location was statistically significant for aspiration biopsy (χ^2=8.01; p=0.018); for SDC, this dependence was even more pronounced (χ^2=10.83; p=0.004), and for hysteroscopic biopsy, the association also remained statistically significant (χ^2=6.90; p=0.032). Consequently, the location of the tumor should be considered one of the factors determining the choice of method for preoperative morphological verification.

4. Conclusions

The only statistically significant difference between the groups was in regard to morphological verification prior to treatment, which was performed more frequently in the cases of uterine sarcoma. The comparative analysis conducted shows that the diagnostic value of preoperative morphological verification of UtS is determined not only by the method of obtaining the specimen but also, to a significant extent, by the anatomical type of tumor growth.

Based on the study, it can be concluded that a negative result of endometrial aspiration biopsy or SDC, in the presence of MRI/ultrasound findings suspicious for an intramural mass, should not serve as a basis for ruling out uterine sarcomas. On the contrary, this combination of results justifies the need for further comprehensive evaluation using imaging findings and, in carefully selected cases, obtaining tissue directly from the tumor.

Conflict of Interests' Statement

The authors declare no conflict of interest.

This study does not include the involvement of any budgetary, grant or other funds.

The article is published for the first time and is a part of scientific work.

ACKNOWLEDGEMENTS

The authors express their gratitude to the management of the Republican Specialized Scientific-Practical Medical Center of Oncology and Radiology for the material provided for our study.

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